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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,648	12/02/2003	Elias J. Corey	006447/00001	4526

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BANNER & WITCOFF, LTD.
28 STATE STREET
28th FLOOR
BOSTON, MA 02109-9601

EXAMINER	
HUMPHREY, DAVID HAROLD	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 02/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/725,648	COREY, ELIAS J.	
	Examiner	Art Unit	
	David Humphrey	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-10 are pending.

Claims 1-10 are examined on the merits.

Sequence Compliance

2. The specification and claims are objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific sequences in the specification and the claims. See 37 CFR § 1.821(d). For example, the amino acid sequence of Peptide YY on page 6 does not contain a sequence identification number. Full compliance is required in response to this Action. A reply that fails to comply will be considered to be non-responsive and may result in abandonment of this application.

Claim Objections

3. Claims 1-10 are objected to because of the following informalities: it is not clear from the format of claims 1-10 if the screening test is a product or a method. However, since method steps are recited, Claims 1-10 are drawn to a colon cancer screening "method" for purposes of examination. Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-10 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue' not 'experimentation'. " (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention and breadth of the claims: The claims are drawn to a colon cancer screening test comprising the steps of establishing a baseline level of Peptide YY in a body fluid sample from a mammalian patient, comparing the level of Petpide YY in a subsequent sample, wherein an elevated level of Peptide YY in the subsequent sample indicates a positive result for colon cancer. Claims 2 and 3 recite the method wherein determination of Peptide YY levels is preceded by an overnight fast. Claims 4 and 5 recite the method wherein the Peptide YY levels are repeated on a time period selected from monthly, quarterly, semi-anally, and annually. Claims 6, 7, and 8, recite the method wherein the body fluid sample is blood, plasma, intestinal fluid, or fecal fluid. Claims 9 and 10 recite the method wherein the PYY levels are measured by a standard protocol for peptide analysis such as radioimmunoassay (RIA), enzyme linked immunoassay (ELISA), automated high performance liquid chromatographic analysis, other analytical chromatographic protocols, capillary electrophoresis, and mass spectroscopy. Thus, the claims encompass methods of quantifying the amount of Peptide YY in a body fluid to diagnose colon cancer in patients.

The state of the prior art and the predictability of the prior art: Takatoh et al. (Acta Pathol. Jpn. 37(5): 737-746, 1987) teach that Peptide YY (PYY) first isolated in 1980, is found in gastrointestinal endocrine tumors and may be used as one of the markers of rectal endocrine tumors, see page 737, Abstract, last sentence; Introduction, lines 3 and 4.

However, the findings of this early study were not supported by the more recent work of others such as El-Salhy et al (Peptides 23: 397-402, 2002). El-Salhy et al.

teach that although the number of PYY cells in the colons of rats has been reported to be high, the concentration of PYY in tissue extracts of the colon of rat adenocarcinoma was not statistically significant, though it was higher than in controls, see page 400, Section 5, lines1-5. El-Salhy et al. further teach that in patients with colorectal carcinoma, neither the number of PYY cells nor the concentration of PYY in the colon is affected, see page 400, Section 5, lines 5-7. In addition, El-Salhy et al. teach that although PYY receptors have been demonstrated in colonic adenocarcinoma cell lines, PYY has been found to exert no direct growth regulator effect on colon cancer cell lines, see page 400, Section 5, lines 8-11. El-Salhy et al. conclude that putting these findings together, it seems unlikely that PYY is engaged in the development and growth of colorectal carcinoma, see page 400, Section 5, lines 11-13.

Tseng et al. (Peptides 23: 389-395, 2002) teach that PYY is a naturally occurring gut hormone with mostly inhibitory actions on multiple tissue targets and a decreased expression of PYY may be relevant to the development and progression of colon cancer, see page 389, Abstract, lines 1-3. Tseng et al. teach that although PYY-positivity was observed in 15% of all rectal carcinoids examined, PYY cells were far outnumbered by cell staining for other gut hormones, see page 390, left column, lines 1-3. Tseng et al. teach that a subsequent study using more specific antibody techniques demonstrated 80% or rectal carcinoids examined were PYY-positive. Nevertheless, within each specimen, PYY-cells represented a minority in a heterogenous tumor population and in fact, adjacent normal mucosa demonstrated higher number of positive cells, see page 390, left column, lines 3-9. Tseng et al. further teach that the later

finding was elaborated on by another study which showed a prevalence of PYY expression in normal cells and another related peptide, pancreatic polypeptide, a related peptide, was expressed in carcinoid cells, see page 390, left column, lines 10-13.

Contrary to the findings of Takatoh, Tseng et al. teach that PYY tissue concentrations of polyps and carcinomas was significantly lower than in control tissue at all regions studied, see page 390, right column, Section 3.1, second paragraph, lines 3-7. These findings were also confirmed by two independent laboratories, see page 390, right column, Section 3.1, second paragraph, lines 7-8. Tseng et al. teach that villous polyps, which have high malignant potential, showed 7-fold less PYY per gram of tissue versus benign hyperplastic polyps, see page 390, right column, Section 3.1, second paragraph, last sentence.

The relationship between known colon cancer risk factors and PYY were also studied. It is known that the incidence of colon cancer increases with patient age. Tseng et al. teach PYY concentrations in the colon were followed from neonatal development to old age in two strains of rats and that PYY levels decreased in a stepwise fashion from 30 days postnatal to senescence at 2 years of age, see page 390, right column, Section 3.1, third paragraph, lines 1-5.

Since the art teaches that PYY levels decrease in colon cancer, one skilled in the art would not expect to detect increased PYY levels in the blood as an indication of colon cancer. Koch et al. (Am. J. Gastroenterol. 82(4): 321-326, 1987) teach that the concentrations of Peptide YY in the serum of healthy controls and patients with

adenocarcinoma of the rectum both fall within the same range, 50 to 260 pg/ml, see Abstract, lines 8-10.

Others teach that increased PYY peptide concentration may provide an anti-tumor effect. McFadden (U.S. Patent 5,574,010, patent date November 12, 1996) teaches contacting a tumor with PYY to reduce tumor cell proliferation, see Abstract.

Therefore, based on the teachings described above, one of ordinary skill in the art would conclude that the prior art is unpredictable and provides data that a decrease, not an increase, in PYY levels is detected in tissues of colon cancer patients. Furthermore, no difference in PYY levels between normal patients and colon cancer patients is detected in the blood.

The guidance presented by the specification and the presence of working examples: There is limited guidance provided in the specification. Applicants have provided no data and no working examples in the specification. Applicants have not demonstrated that PYY secretion is enhanced in cancerous colon cells or that the levels of PYY are increased in the blood of cancer patients. Applicants merely state that "it is logical, therefore, that the production and secretion of PYY would be enhanced in cancerous colon cells, especially since PYY stimulates proliferation of gastrointestinal mucosa", see Specification, page 8, second complete paragraph, lines 5-7. The specification further states that "the most important connection between colon cancer and PYY overproduction comes from the observation that weight loss frequently occurs during the progression of colon cancer", see Specification, page 8, third complete paragraph, lines 2-5. However, Applicants' logic and observations are not in

concordance with the prior art, which does not teach the elevated levels of PYY in colon cancer.

Thus, the present invention is thus merely a "gedanken" experiment based on a hypothetical connection between weight loss due to increased PYY production and weight loss due to colon cancer. The prophetic teachings of the specification are not supported by the art. In fact, prior art teaches away from the claimed invention.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed inventions without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support Applicant's claim to a method of using an increase in PYY level to screen for colon cancer. All of the factors considered in the sections above, underscores the criticality of providing working examples in the specification for an unpredictable art such as screening for colon cancer.

Quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the Wands factors considered above, one of ordinary skill in the art would conclude that a method of screening for colon cancer using Peptide YY would require undue experimentation in order to use the invention as claimed by the Applicants.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Humphrey whose telephone number is (571) 272-5544. The examiner can normally be reached on Mon-Fri 8:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Humphrey, Ph.D.

February 14, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER